REMARKS

Claims 11-27 and new claims 28-58 are pending. By the foregoing amendment, the specification has been amended to correct an error in generic formula I to add an "A" substituent. The correct formula, including the "A" substituent, is shown in U.S. Patent 5,607,942 which is incorporated by reference at the top of p. 6. Correction is also made to the chemical formula submitted in the response filed March 9, 2006. In particular, the March 9, 2006 amendment inadvertently included an extraneous double bond in the fused ring on the right-hand side of the structure. The originally filed specification, at the bottom of page 5, showed the correct double bond configuration (but failed to include the –COOH moiety that was added by the March 9, 2006 amendment).

New dependent claims 28-58 depend from allowable claims 11 or 12 and do not enlarge the scope of the allowed claims. New claims 28-57 are allowable over the prior art for at least the same reasons applicable to allowable claims 11 and 12. Support for the new claims is found throughout the specification, with particular reference to the disclosure highlighted in the table below. No new matter is added.

Claim	**Limitation(s)**	**Support in Specification**
28	moxifloxacin at a concentration of greater than 0.1 wt. %	p. 7, lines 14-16; pp. 11-12, Examples 1-4
29	moxifloxacin at a concentration of at least 0.35 wt. %	p. 7, lines 14-16; pp. 11-12, Examples 1 & 3
30	moxifloxacin at a concentration of about 0.35 wt. %	pp. 11-12, Examples 1 & 3
31	moxifloxacin at a concentration of 0.35 to 1 wt. %	p. 7, lines 14-16; pp. 11-12, Examples 1 & 3
32-35	applied to the eye in connection with the treatment of conjunctivitis	p. 3, lines 19-20
36	contains sodium chloride	p. 11, Example 2
37	viscosity enhancing agent surfactant	p. 10, lines 10-17 p. 10, lines 4-8
38	pH in the range of from 4.5 to 8.0	p. 9, lines 19-20

39	pH in the range of from 5.5 to 8.0	p. 9, lines 19-20; p. 11, Example 2 (pH 5.5)
40	osmotic value compatible with the aqueous humor of eye and ophthalmic tissue, about 200 to about 400 milliosmoles per kilogram of water	p. 9, lines 20-24
41	osmotic value compatible with the aqueous humor of eye and ophthalmic tissue, about 200 to about 300 milliosmoles per kilogram of water	p. 9, lines 20-24
42	osmotic value about 300 milliosmoles per kilogram of water	p. 9, line 24
43	preservative at from 0.001 to 1.0 wt. %	p. 9, line 27 to p. 10, line 2
44	sterile solution provided in a multi-dose form	p. 9, lines 10-11 and 26-27
45	applied to the eye in connection with the treatment of conjunctivitis	p. 3, lines 19-20
46-50	inhibits the growth of *S. aureus*, *S. epidermidis*, *S. pneumoniae*, *P. aeruginosa*, *H. influenzae* provides moxifloxacin concentration in lacrimal fluid and aqueous humor at or above MIC_{90} level	Table at bottom of p. 6 p. 7, lines 4-8
51	sterile solution pH 4.5 to 8.0 osmotic value 200 to 400 milliosmoles per kg water moxifloxacin at a concentration of 0.35 to 1 wt. %	p. 9, lines 10-11 p. 9, lines 19-20 p. 9, lines 20-24 p. 7, lines 14-16; pp. 11-12, Examples 1 & 3
52	pH in the range of from 5.5 to 8.0	p. 9, lines 19-20; p. 11, Example 2 (pH 5.5)
53	osmotic value about 300 milliosmoles per kg water	p. 9, line 24
54	contains sodium chloride	p. 11, Example 2
55	viscosity enhancing agent surfactant	p. 10, lines 10-17 p. 10, lines 4-8
56	applied to the eye in connection with the treatment of conjunctivitis	p. 3, lines 19-20
57	inhibits the growth of *S. aureus*, *S. epidermidis*, *S. pneumoniae*, *P. aeruginosa*, and/or *H. influenzae*	Table at bottom of p. 6
58	composition is applied to the eye in connection with an ophthalmic surgical procedure	p. 3, lines 3-5 and 21-22

Applicants wish to thank Examiner Fay for the courtesies extended to their representatives Dale Hoscheit and Paul Rivard during a personal interview on September 12, 2006. During the interview, Ms. Fay was presented with and reviewed a copy of new claims 28-58 and the table showing support for the new claims in the specification, both as appear above.

Applicants representatives also discussed the documents filed in the European opposition, which were submitted in the Information Disclosure Statement filed August 31, 2006. Ms. Fay acknowledged receipt of the opposition papers and requested that Applicants provide a brief summary of the issues involved in the European opposition concerning prior art to assist in her review thereof. Such a summary is provided below. The oral argument was held in Munich on September 14, 2006 and the opposition panel upheld the European patent as granted. A copy of this patent, European Patent 1,117,401 B, is attached hereto.

The opponent in its opposition paper dated August 23, 2004 argued, "According to the opposed Patent itself . . . and to the Patentee's submission during prosecution . . . the use of quinolone antibiotics, such as ciprofloxacin, ofloxacin, norfloxacin, etc. in ophthalmic pharmaceutical compositions was the current state of the art." (p. 3). U.S. Patent 5,607,942 was argued to give "a direct incentive towards Moxifloxacin since, out of the many compounds disclosed therein, D1 [the '942 patent] has specifically claimed Moxifloxacin itself (see claim 2)." (p. 4). The opponent further argued that "the presently claimed range of concentrations was fully obvious for ophthalmic compositions in view of the disclosure of D3 [WO 90/09133 A], wherein concentrations are disclosed in the range of 0.01 to 2.0 wt% . . ." (p. 5). According to the opponent,

> In view of the foregoing it appeared thus that testing Moxifloxacin, the representative of the newest generation of quinolone antibiotics already claimed as such in D1, in ophthalmic preparations, in the same conditions as already known for the quinolone antibiotics of the former generation from D3, was a fully "**obvious-to-try**" operation. Therefore, any possible improved effect deriving from such an obvious-to-try activity can just be a "***bonus effect***" unsuitable to support the inventive activity according to the established EPO case law.

Opp. at p. 6 (bold and italics in original; underlining added). Of course, "obvious to try" is not the law in the United States,[1] and unexpected results can be used to establish non-obviousness.[2] Even under the European standard, the opposition panel upheld the patent as granted.

As discussed in the Declaration of David W. Stroman, Ph.D., which was submitted by Applicants in the European opposition proceeding and provided to Examiner Fay, the Survey of Ophthalmology article[3] summarizes the results of numerous studies on the pharmacokinetics of moxifloxacin conducted by Alcon scientists as well as other scientists and physicians. Table 3 from the published article, reproduced below, compares permeability properties of moxifloxacin (the antibiotic present in VIGAMOX®), to those of gatifloxacin (the antibiotic present in Zymar®), ciprofloxacin (the antibiotic present in Ciloxan®), ofloxacin (the antibiotic present in Ocuflox®), norfloxacin (the antibiotic present in Chibroxin®), levofloxacin (the antibiotic present in IQUIX®), and lomefloxacin (the antibiotic present in Maxaquin®):

Fluoroquinolone	Molecular Weight	Aqueous solubility (%)	MDCK Permeability (cm/s) × 10^7	Corneal Permeability[$] (cm/s) × 10^7	Lipophilicity C-7, π
Moxifloxacin	401.4	>6.43[$$]	35.2	15.8	0.24
Gatifloxacin	375.4	0.21	10.3	4.6	0.11
Ciprofloxacin	331.3	0.02	4.5	2.46	−0.35
Ofloxacin	361.4	0.35	15.1	6.78	0.06
Norfloxacin	319.3	0.05	3.3	1.63	−0.35
Levofloxacin	361.4	1.85[$$]	16.4	6.95	0.06
Lomefloxacin	351.3	0.13	6.6	3.58	0.11

[$] Data for moxifloxacin and gatifloxacin were estimated by linear regression; Data for remaining five fluoroquinolones were from Fukada and Sasaki.[5]

[$$] After 13 weeks of mixing.

As can be easily seen from this table, moxifloxacin shows a significantly higher penetration into the eye than each of these commercially available fluoroquinolones. Further

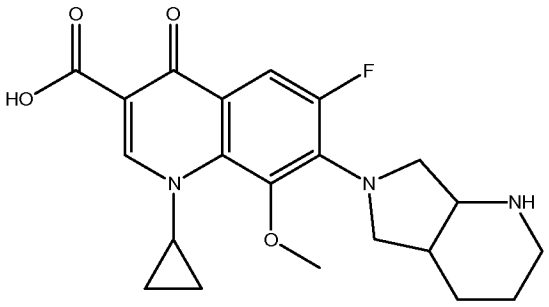
[1] *In re O'Farrell*, 853 F.2d 894, 7 U.S.P.Q.2d 1673 (Fed. Cir. 1988).

[2] *See, e.g., In re Chupp,* 816 F.2d 643, 646, 2 U.S.P.Q.2d 1437, 1439 (Fed. Cir. 1987).

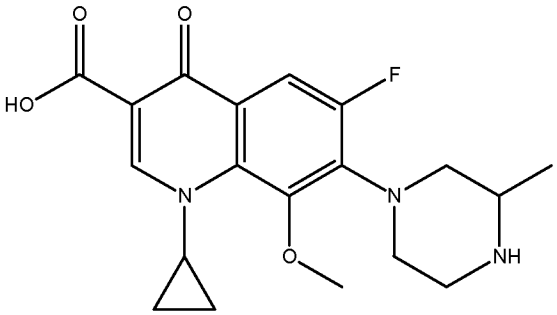
[3] Survey of Ophthalmology, 50, Supp. 1, Nov. 2005.

evidence of unexpected results can be found in Applicants' response filed in the opposition on June 28, 2005 as well as in the Stroman declaration.

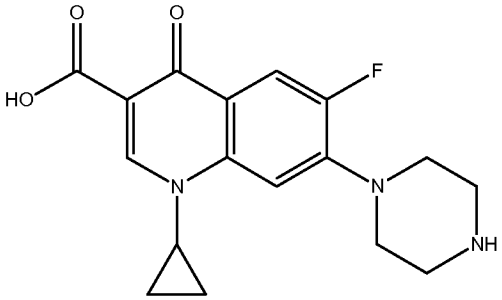
The chemical structure of each of these fluoroquinolones is illustrated below for the Examiner's convenience:



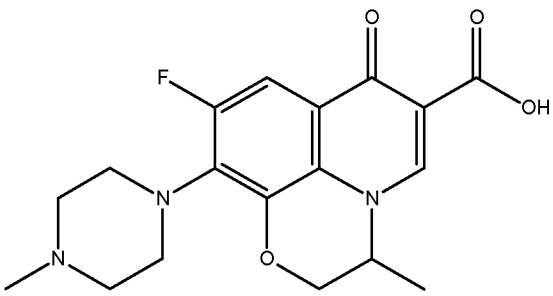
Moxifloxacin



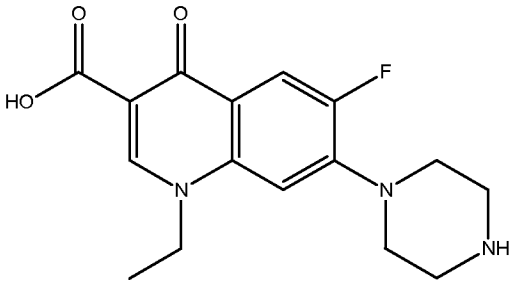
Gatifloxacin



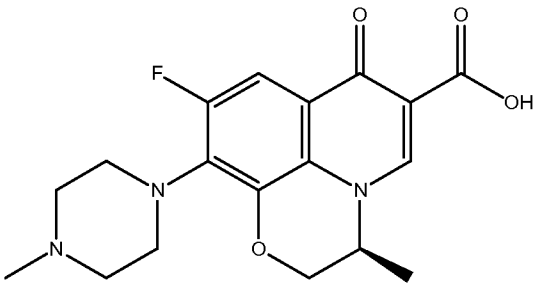
Ciprofloxacin



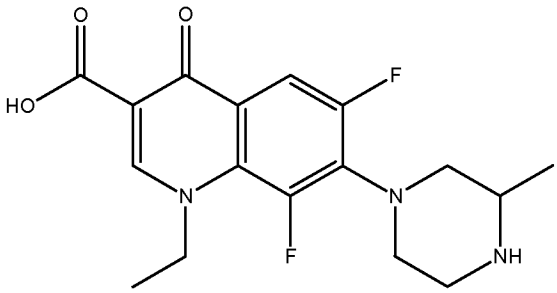
Ofloxacin



Norfloxacin



Levofloxacin



Lomefloxacin

In its reply, the opponent did not present any data but instead only criticized the Patentee's data (see letter from opponent dated July 11, 2006). The opponent argued that the differences in tear film concentrations between moxifloxacin and ofloxacin were not statistically significant. As discussed at the September 12, 2006 interview, the meaningful comparison is the ability of moxifloxacin to penetrate the cornea to reach intraocular tissues. As shown in the table above, moxifloxacin reaches the intraocular fluid and intraocular tissues at much higher levels than does ofloxacin.

The foregoing summary is intended to assist the Examiner in her review of the opposition materials. The Examiner is encouraged to review the opposition documents in their entireties. Applicants note again that the arguments presented were not successful in Europe.

Respectfully submitted,

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Date: September 15, 2006

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